REMARKS

I. Support for the Amendments

Claims 1, 3, and 12 were previously in the application. Claim 3 has been amended, claims 13-16 have been added, and claims 1 and 12 have been canceled without prejudice to their pursuit in an appropriate continuation or divisional application. Claims 3 and 13-16 are currently in the application. Claim 3 is the independent claim.

Support for amended claim 3 and for new claims 13-16 can be found in the original specification and claims.

Additional support for amended claim 3 and for new claims 13-16 can be found, e.g., from page 35, line 34, to page 36, line 4; on page 36, lines 13-15; from page 37, line 1, to page 46, line 13; and in the Examples.

II. Status of the Claims

Claims 1-3 were originally in the application, with claims 1 and 3 being the independent claims. Claims 1-3 were subject to an Election/Restriction Requirement, and claims 1 and 3 (Group I) were elected with traverse.

Claims 1, 3, and 12 were previously in the application. Claim 3 has been amended, claims 13-16 have been added, and claims 1 and 12 have been canceled without prejudice to their pursuit in an appropriate continuation or divisional application. Claims 3 and 13-16 are currently in the application. Claim 3 is the independent claim.

III. The Rejection of Claims 1, 3, and 12 is Traversed in Part, Accommodated in Part, and Rendered Moot in Part

The Examiner has rejected claims 1, 3, and 12 under 35 U.S.C. §101 alleging that they are drawn to an invention with no apparent or disclosed specific and substantial credible utility. Applicants respectfully disagree, but have canceled claims 1 and 12 and amended claim 3.

The Patent Office alleges:

> ....Whereas the instant application in combination with the Tan et al. publication (GENOMICS 52:223-229, 01 Sept. 1998) has provided a description of an isolated DNA encoding a putative receptor protein identified therein as "FM-3" and having "modest sequence identity to both the GHS-R and neurotensin-R", and the protein encoded thereby, it does not identify a specific biological role for this protein or its significance to a particular disease, disorder of physiological process which one would wish to manipulate for a desired clinical effect through the application of an agonist or antagonist thereto.
>
> The text on page 35 of the instant specification expressly identifies "FM-3" as "an orphan receptor protein". Therefore, a method that serves no further purpose than the further characterization of an orphan receptor lacks a specific and substantial utility because it is employing that receptor as nothing more than the object of further research. Because the instant specification has failed to credibly identify a physiological process which has been shown to be influenced by the activation or inhibition of a putative receptor protein of the instant invention an artisan would have no way of predicting what effects the administration of that ligand to an organism would have. If one can not predict the effects that the administration of a ligand of the putative receptor of the instant invention is going to have on an organism then it is unclear as to what practical benefit is derived by the public from the identification of that ligand. In essence, the instant claims are drawn to a method that consists of nothing more than the further characterization of a protein of as yet undetermined significance. [Par. 5, pp. 2-3.]

Citing *Brenner v. Manson* (148 U.S.P.Q. 689 [U.S.Sup.Ct., 1966]), the Patent Office continues:

....The instant claims are drawn to a method of characterizing a protein of as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the instant specification as "FM-3", the information produced by that analytical process lacks a practical utility.

The protein employed in the method of the instant invention is a compound known to be structurally analogous to proteins which are known in the art as G protein-coupled receptors. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it or a process that only serves to further characterize it. To employ a protein of the instant invention in the identification of substances which inhibit or induce its activity is clearly to use it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. It was well known in the art long before the making of the instant invention that G protein-coupled receptors can be stimulatory or inhibitory, depending upon the particular receptor and the cell in which it is expressed. To employ an assay of the instant invention in the identification of substances that inhibit or induce the activity of an "FM-3" protein without knowing the physiological consequence of that inhibition or induction is clearly to use that protein as the object of further research, which has been determined by the courts to be a utility which, alone, does not support patentability. As indicated above, an invention must have a specific and substantial utility "in currently available form", which precludes the need for further research, if that research is needed to establish a utility for the claimed invention. Since the instant specification does not disclose a credible "real world" use for the claimed assay then it is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful. [Par. 5, pp. 4-5.]

Claims 1 and 12 have been canceled and the rejection is rendered moot with respect to these claims.

With respect to amended claim 3 and new claims 13-16, Applicants respectfully assert that the advantage of the present invention as described in amended claim 3 and in new claims 13-16 lies in that it substantially reduces the number of the ligand candidates to be considered in the first step based on a reasonable standard (i.e., an agonist activity, homology, etc.) such that the determination of a ligand for an orphan receptor protein in the second step becomes much more efficient and reliable. The reasonable standard relies, in part, on a common structure that is shared among the compounds selected based on the

presence of an agonist activity. The common structure is verified based on the "homology" or "similarity" in the structure of the test compounds.

One feature of the present invention lies in the reduction of the number of the candidate compounds based on the reasonable standard such that the determination of a ligand for an orphan receptor protein is much more efficient and reliable. The level of the reduction of the number can vary and is decided by the practitioner. Thus, those skilled in the art can "set" the level of the desired reduction by adjusting the degree of the homology or the similarity in the structure as appropriate for a chosen purpose. In this sense, the "common structure" can be freely set as appropriate by those skilled in the art depending on the purpose, the available techniques or resources, the amount of time available, and the like, and thus the "common structure" is clear to one of ordinary skill in the art based on the present specification in light of general knowledge within the field.

Moreover, given the isolation, identification, and sequencing of many biological compounds to date and the widespread availability of nucleotide and protein sequence databases, such as BLAST, Applicants suggest that, in some cases, identification of a ligand of an orphan receptor protein could assist in the identification of the orphan receptor protein and/or in the understanding of an additional role the ligand.

The amended claims are drawn to a method of identifying a ligand for an orphan receptor protein, and one purpose of the present invention is to establish an efficient and reliable method for screening compounds and their salts, which promote or inhibit a function of an orphan receptor protein. The specific and substantial credible utility is apparent or disclosed in the present specification.

Claims 1 and 12 have been canceled and the rejection is rendered moot with respect to these claims.

Applicants respectfully submit that the present amendments to claim 3 accommodate the Examiner's rejection of this claim under 35 U.S.C. §101, thereby placing this claim in condition for allowance.

IV. The Rejection of Claims 1, 3, and 12 under 35 U.S.C. §112, First Paragraph, is Traversed in Part, Accommodated in Part, and Rendered Moot in Part

The Examiner has rejected claims 1, 3, and 12 under 35 U.S.C. §112, first paragraph, alleging failure to teach how to use the instant invention for the reasons given in the previous section with regard to the rejection of these claims under 35 U.S.C. §101. Applicants respectfully disagree, but have canceled claims 1 and 12 and amended claim 3.

The Patent Office alleges:

> Claims 1, 3 and 12 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

Applicants disagree, but respectfully submit that the amendments to claim 3 place this claim in condition for allowance for the reasons given in the previous section with regard to the rejection of this claim under 35 U.S.C. §101.

Claims 1 and 12 have been canceled and the rejections of these claims are rendered moot.

Applicants respectfully submit that the present amendments to claim 3 accommodate the Examiner's rejection of these claims under 35 U.S.C. §112, first paragraph, thereby placing this claim in condition for allowance.

V. The Rejection of Claims 1, 3, and 12 under 35 U.S.C. §112, Second Paragraph, is Accommodated in Part and Rendered Moot in Part

The Examiner has rejected claims 1, 3, and 12 under 35 U.S.C. §112, second paragraph (pp. 4-6). The Examiner's rejection is outlined in paragraph 7 on pages 6-7.

Applicants respectfully submit that the amendments to claim 3 address these points and that these amendments accommodate the Examiner's rejections with respect to claim 3.

Claims 1 and 12 have been canceled and the rejection is rendered moot with respect to these claims.

Applicants respectfully submit that the present amendments to claim 3 accommodate the Examiner's rejection of these claims under 35 U.S.C. §112, second paragraph, thereby placing this claim in condition for allowance.

VI. The Rejection of Claims 1, 3, and 12 under 35 U.S.C. §102(a) or §103 is Rendered Moot

The Examiner has rejected claims 1, 3, and 12 "under 35 U.S.C. 102 (a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over the Tan et al.

publication (GENOMICS 52:223,229, 01 Sept. 1998)." Applicants respectfully disagree, but have canceled claims 1 and 12 and amended claim 3.

Citing the text in the second full paragraph on page 228 of Tan et al., the Patent Office alleges:

> Whereas it is unclear if Tan et al. employed a comparative step in the assays described therein, one of ordinary skill would have found it *prima facie* obvious to have included such a step in that assay because it was well known in the art at the time of the Tan et al. publication that most, if not all, mammalian cells express a variety of endogenous G protein-coupled receptors. It is unclear how Tan et al. would have attributed a measured change in a cellular parameter such as binding or calcium mobilization to the action of that compound upon FM-3, to the exclusion of any or all of the endogenous G protein-coupled receptors that might be expressed by a test cell; in the absence of a comparative step that employs a cell that is otherwise identical to the test cell except for the absence of FM-3. [Par. 8, p. 8.]

As amended, claim 3 currently reads as follows:

> 3 (currently amended). A method of identifying a ligand for an orphan receptor protein, comprising the steps of:
>
> (a) pre-selecting a ligand candidate, wherein step (a) comprises:
>
> (i) comparing a cell stimulating activity of a test compound between a sample wherein the test compound is brought in contact with a cell expressing an orphan receptor or its cell membrane fractions, and a sample wherein the test compound is brought in contact with a cell which does not express the orphan receptor or its cell membrane fractions;
>
> (ii) selecting the test compound that has an agonist activity at the orphan receptor;
>
> (iii) predicting a common structure that is present in the thus selected test compounds based on homology or similarity among the structures; and
>
> (iv) obtaining a ligand candidate that contains the common structure; and
>
> (b) determining a ligand from among one or more ligand candidates, wherein step (b) comprises:
>
> (i) comparing a cell stimulating of a ligand candidate, which is measured when the ligand candidate is brought in contact with a cell expressing the orphan receptor or its cell membrane fractions, with a

cell stimulating activity of a test compound, which is measured when the test compound is brought in contact with a cell expressing the orphan receptor or its cell membrane fractions; and

(ii) selecting the ligand candidate that has specific binding to the orphan receptor as a ligand of the orphan receptor.

In view of the amendments to claim 3, Applicants respectfully submit that the rejection based on the Tan reference is rendered moot since the present language of claim 3 does not specifically relate to identification of a ligand for FM-3.

Claims 1 and 12 have been canceled and the rejections of these claims are rendered moot.

Applicants respectfully submit that the present amendments to claim 3 accommodate the Examiner's rejection of this claim under 35 U.S.C. §102(a) and/or103(a), thereby placing these claims in condition for allowance.

VII. Additional Request for Filing Receipt

Applicants have not yet received an Official Filing Receipt. Applicants have filed Requests for an Official Filing Receipt on September 21, 2004, on February 8, 2005, and on October 12, 2005, but have not received a response. Applicants respectfully request any assistance the Examiner could provide in obtaining an Official Filing Receipt.

CONCLUSION

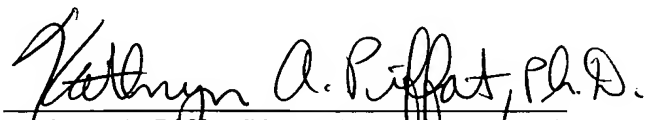
It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants respectfully request a one-month extension of time for the Amendment and accompanying materials and submit the appropriate fee herewith. If an additional extension of time is required, Applicants hereby request the Examiner to consider this a conditional petition for an additional extension of time. Although it is not believed that any additional fee (in addition to the fee concurrently submitted) is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

Date: August 10, 2006



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